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Asthma control in elderly asthmatics. An Italian observational study

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KEYWORDS
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Summary
Background: The exponential increase of individuals aged >64 yrs is expected to impact the burden of asthma. We aimed to explore the level of asthma control in elderly subjects, and factors influencing it.
Methods: A multicenter observational study was performed on consecutive patients >64 years old with a documented physician-diagnosis of asthma. Sixteen Italian centers were involved in this 6-month project.
Findings: A total of 350 patients were enrolled in the study. More than one-third of elderly asthmatic patients, despite receiving GINA step 3–4 antiasthmatic therapy, had an Asthma Control Test score ≤19, with a quarter experiencing at least one severe asthma exacerbation in the previous year. Twenty-nine percent of patients (n = 101) were classified as having

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Asthma-COPD Overlap Syndrome (ACOS) due to the presence of chronic bronchitis and/or CO lung diffusion impairment. This subgroup of patients had lower mean Asthma Control Test scores and more exacerbations compared to the asthmatic patients (18 $\pm$ 4 compared to 20 $\pm$ 4, $p < 0.01$, and 43% compared to 18%, $p < 0.01$, respectively). Modified Medical Research Council dyspnea mMRC scores and airway obstruction, assessed on the basis of a FEV_1/FVC ratio below the lower limit of normal, were more severe in ACOS than in asthma, without any difference in responses to salbutamol. In a multivariate analysis, the mMRC dyspnea score, FEV_1% of predicted and the coexistence of COPD were the only variables to enter the model. *Interpretation:* Our results highlight the need to specifically evaluate the coexistence of features of COPD in elderly asthmatics, a factor that worsens asthma control.

Introduction

In high income countries, the prevalence of asthma in older adults (>64 year) is reported to range between 6% and 10%, not different from that of young adults [1]. Due to a predicted 100% increase in people aged >64 years in the next 20 years [2], it is reasonable to expect a rise in the impact of asthma in older people. Nevertheless, asthma in the elderly is often underdiagnosed [3] or misdiagnosed [4], and the mortality for asthma in this age range remains high [1]. Moreover, the burden of concomitant asthma and COPD is relevant [5], given the reported overlap rate of 40%—60% in elderly subjects [6]. In particular, the coexistence of asthma and COPD appears to negatively affect overall symptom control as well as the response to treatment [7]. Nevertheless, the coexistence of asthma with COPD is still an exclusion criterion for participating in clinical trials, and guidelines on this topic are based only on expert opinions. An important contribution to understanding overlap syndrome comes from Spanish investigators who recently published a consensus document on the clinical phenotype called "Overlap Phenotype COPD-Asthma" [8]. In particular, overlap syndrome appears to negatively affect the response to treatment and overall symptom control.

The mainstay of asthma management is to achieve and maintain control of the disease. Pharmacological control of symptoms can be influenced by age-related factors, such as the more frequent occurrence of comorbidities and patients having prescriptions for multiple drugs. Comorbidities are considered one of the hallmarks of the geriatric patient, and they contribute to the complexity of the elderly and may account for the poorer outcomes of asthma in this group compared to younger patients. The presence of comorbidities has been demonstrated to influence quality of life in adults with asthma [9], which in turn can affect adherence to treatments. In this context, specific comorbidities may also impair the ability to use inhalation devices, for example, in patients who suffer from arthritis.

The impact of comorbidities on elderly asthmatic patients has never been specifically addressed, especially with regard to the coexistence of COPD. Herein, we report the results from the Italian observational study ELderly Subjects with Asthma (ELSA), which was carried out by a network of pulmonology and allergy clinics with the aims of assessing overall asthma control and respiratory function in patients with and without coexisting COPD, and investigating factors associated with worse control.

Methods

The ELSA Survey was carried out between October 2012 and March 2013 in 16 Italian Health Service pulmonology and allergy clinics, whose members participated in the task force promoted by the Allergy Study Group of the Italian Society of Respiratory Medicine (Società Italiana di Medicina Respiratoria, SIMeR). To be consecutively enrolled in the study, subjects had to have a diagnosis of asthma by a physician, based on the 2012 GINA guidelines [10], and be 65 years of age or older. Data from each center were collected by the coordinating center, Pietra ligure (Pulmonology Division of S. Corona Hospital), which was also responsible for quality control and final processing of the data. The study was approved by local Ethics Committees.

For each asthmatic subject, the investigators recorded the following information using a standardized questionnaire: 1) age, sex, height, and weight; 2) smoking status; 2) age of asthma onset, defined as the age when the patient received a physician's diagnosis of asthma, properly documented in their medical record; 3) chronic bronchitis status, defined as "symptomatic mucus hypersecretion with cough and sputum daily for at least 3 months over 2 years" [11]. In addition, patients were given the modified Medical Research Council (mMRC) dyspnea scale [12] and the Asthma Control Test (ACT) [13]. Finally, the number of severe asthma exacerbations (SAEs) in the previous year, defined as "an asthma exacerbation requiring systemic corticosteroids for at least three days and/or hospitalization" [14]; the use of inhaled corticosteroids (ICS) with the daily dosage expressed as a low, medium, or high dosage of beclomethasone dipropionate, CFC or equivalent according to GINA classification [10], and the use of fixed inhaler combinations (ICS plus Long Acting Beta Agonists, LABA) were recorded. Comorbidities were inferred by recording concomitant drug prescriptions for other diseases (arterial hypertension, chronic heart disease, diabetes, gastroesophageal reflux, and osteoporosis). The investigators were also required to diagnose the occurrence of the overlap condition (asthma and concomitant COPD) according to current guidelines [10,11].

All patients underwent skin prick testing with a standard panel of airborne allergens (grasses, pellitory, ragweed, birch, cypressus, olive, dermatophagoides pteronyssinus and farinae, cat and dog epithelia, alternaria tenuis, and aspergillus fumigatus). The test was considered positive if the mean wheal diameter was 3 mm or larger after subtraction of the mean wheal of the negative control [15,16].

Spirometry (forced vital capacity maneuver) was performed according to the standardized technique [17] after a proper wash-out period from bronchodilator drugs. In cases of normal spirometry, a historical reversibility or methacholine bronchoprovocation test was also obtained to further support the diagnosis of asthma. In cases where the airway obstruction defined by the FEV_1/FVC ratio was below the lower limit of predicted values [18], subjects underwent a second spirometric assessment twenty minutes after the administration of 400 mcg of salbutamol by a pressurized metered dose inhaler (pMDI) with a space chamber. The response was calculated as percentage increase in FEV_1 and/or FVC from the baseline value and was considered "non-significant," or in the threshold of natural variability, when the volume increase was $<$200 ml and $<$12% of the baseline value [18]. Moreover, the airway obstruction was considered to be a "fixed airway obstruction" when the post-salbutamol FEV_1/FVC ratio was below the lower limit of the predicted value. In cases where FEV_1 and/or FVC changed by $\geq$200 ml and $\geq$12% of the baseline value, the response was considered "significant," or above the threshold of natural variability [18]. Moreover, it was considered "reversible" if the post-salbutamol FEV_1/FVC ratio reached the normal range, and "non—fully reversible" when the post-salbutamol FEV_1/FVC remained below the lower limit of normal [19]. All patients with smoking habits and non-fully reversible airway obstructions, and those with fixed airway obstructions underwent a single breath CO diffusion test using the standardized technique [20]. The diffusing capacity of the lungs for CO ($D_{L,\,CO}$) was measured by the single breath method [20] and corrected for the hemoglobin level. A $D_{L,\,CO}$ result of $<$80% of the predicted value was considered indicative of emphysema in the absence of anemia or pulmonary fibrosis [18]. Patients were considered to have asthma-COPD overlap in cases of chronic bronchitis and/or an impaired CO diffusion test [11,18] and were referred to as having asthma-COPD Overlap Syndrome (ACOS).

Data analysis

The results are shown as the mean $\pm$ standard deviation (SD), unless otherwise stated. With an approximate expected overlap percentage of 30% between asthma and COPD in patients aged $\geq$65 years [6], 350 subjects were estimated to be needed in order to include at least 100 subjects with overlap. Continuous variables were compared using *t*-tests and dichotomous variables were compared using a chi-square or Fisher's exact test. The relationships between variables were evaluated using Pearson product moment correlation coefficients. Asthma control was defined as well-, partially or poorly controlled for ACT scores of $\geq$20, 16—19, or $\leq$15, respectively [21]. Multivariate linear regression analyses were performed using the ACT score as the dependent variable. A stepwise approach to model building was applied; the model also included those variables yielding *p*-values lower than 0.20 in the univariate analyses. All tests were two-sided, and *p*-values lower than 0.05 were considered statistically significant. Statistical tests were performed using the Statistical Package for Social Sciences (version 19.0; SPSS, Chicago, IL).

Results

A total of 350 elderly subjects with a definite diagnosis of asthma were enrolled. All patients underwent a forced vital capacity maneuver. Table 1 summarizes demographic, clinical and functional data of the study subjects. Those who had never smoked (69%) were more represented than former smokers (27%) and current smokers (4%). Fifty percent of the subjects had a positive skin prick test for airborne allergens, mainly for house dust mites (HDM, 62%). There were more females than males (220 vs 130, $p < 0.001$), with significant and marked differences between genders in smoking habits and mMRC scores. With regard to the outcomes of poor asthma control, an ACT score of $\leq$19 occurred in 39% of the subjects with the presence of at least one SAE seen in 25%.

Asthma therapy

To better characterize asthma therapy, enrolled subjects were divided into two groups: a) those enrolled during a scheduled follow-up visit at the center and named "follow-up," and b) those enrolled at their first visit and named "naïve," referred by general practitioners at the center for respiratory symptoms such as exertional dyspnea (44%), cough (30%), or both (35%), or for a recent "exacerbation" treated as a "severe asthma exacerbation" (2%). In the second group, asthma diagnoses were confirmed after a 6-month follow-up. Fig. 1 shows respiratory drugs recorded at the time of the enrollment visit for "follow-up" and "naïve" subjects.

Asthma-COPD overlap syndrome (ACOS)

Twenty-nine percent of asthmatic subjects ($n = 101$) were considered to also be affected by COPD and were classified as ACOS. Among them, 84% reported chronic bronchitis and 35% demonstrated impaired CO diffusion (54 $\pm$ 9% of predicted, mean $\pm$ SD). Both conditions were present in 22% of the subjects. The physician's diagnosis of asthma-COPD overlap agreed with the diagnosis based on the above-mentioned criteria in 92% of cases. When comparing asthmatics with subjects suffering from ACOS, the latter appeared to be older and were more frequently former smokers than asthmatic subjects. Subjects with ACOS did not differ from those with asthma in the rate of sensitization to airborne allergens, except for a higher rate of HDM sensitization (77% vs 55%, respectively; $p < 0.01$). Subjects with ACOS had higher mMRC dyspnea and lower ACT scores (Table 2). A significantly higher proportion of subjects with ACOS were shown to have experienced one SAE (43% vs 18%, $p < 0.01$) or $\geq$2 SAEs (25% vs 7%, $p < 0.01$) in the previous 12

Table 1 Demographic, clinical and functional data of the study subjects.

	All patients (n = 350)	Female (n = 220)	Male (n = 130)	P
Age, yrs	72 ± 6	72 ± 6	73 ± 6	0.590
BMI, kg/m^2	27 ± 5	28 ± 5	27 ± 4	0.127
BMI≥30, %	24	29	17	0.009
Current smokers, %	4	5	1	<0.001
Former smokers, %	26	14	46	
Never smokers, %	69	79	51	
Pack-years	16 ± 12	18 ± 11	15 ± 12	0.300
Age of onset, yrs	57 ± 18	57 ± 19	58 ± 17	0.457
Asthma duration, yrs	15 ± 18	16 ± 19	15 ± 16	0.594
Sensitized, %	52	53	51	0.912
mMRC, score	1.07 ± 0.89	1.19 ± 0.89	0.86 ± 0.85	0.001
Subjects with SAE,%	25	25	26	0.936
ACT, score	20 ± 4	20 ± 4	21 ± 4	0.036
ACT≤19, %	39	42	35	0.228
FEV_1/FVC, % predicted	88 ± 12	88 ± 12	88 ± 13	0.958
FEV_1, % predicted	83 ± 20	85 ± 20	81 ± 20	0.081
FVC, % predicted	94 ± 16	95 ± 16	91 ± 16	0.021
Comorbidity, %	72	74	67	0.080
Two comorbidities, %	42	49	30	<0.001
≥3 comorbidities, %	13	16	8	0.014

Data are expressed ad mean ± SD if not otherwise stated. Sensitized: to airborne allergens. mMRC: modified Medical Research Council dyspnea score; SAE, Severe Asthma Exacerbation. ACT: asthma control test.

months. Subjects with ACOS had lower airway function as expressed by a lower percentage of predicted FEV_1 and FVC (Table 2), without any difference in asthmatics in the response to salbutamol for FEV_1 (Δ278 ± 146 ml and Δ11 ± 7% vs Δ283 ± 151 ml and 19 ± 12%, respectively). The response to salbutamol for FVC was higher in ACOS than in asthma only when expressed as a percentage value (15 ± 12 vs 11 ± 7, p = 0.009, Δ280 ± 206 ml vs Δ247 ± 190 ml). The percentages of subjects with ACOS with fixed airway obstruction (19%), non-fully reversibility (38%) or reversibility (43%) were not different from that of subjects with asthma (25%, 26%, and 49%, respectively). The ratio of

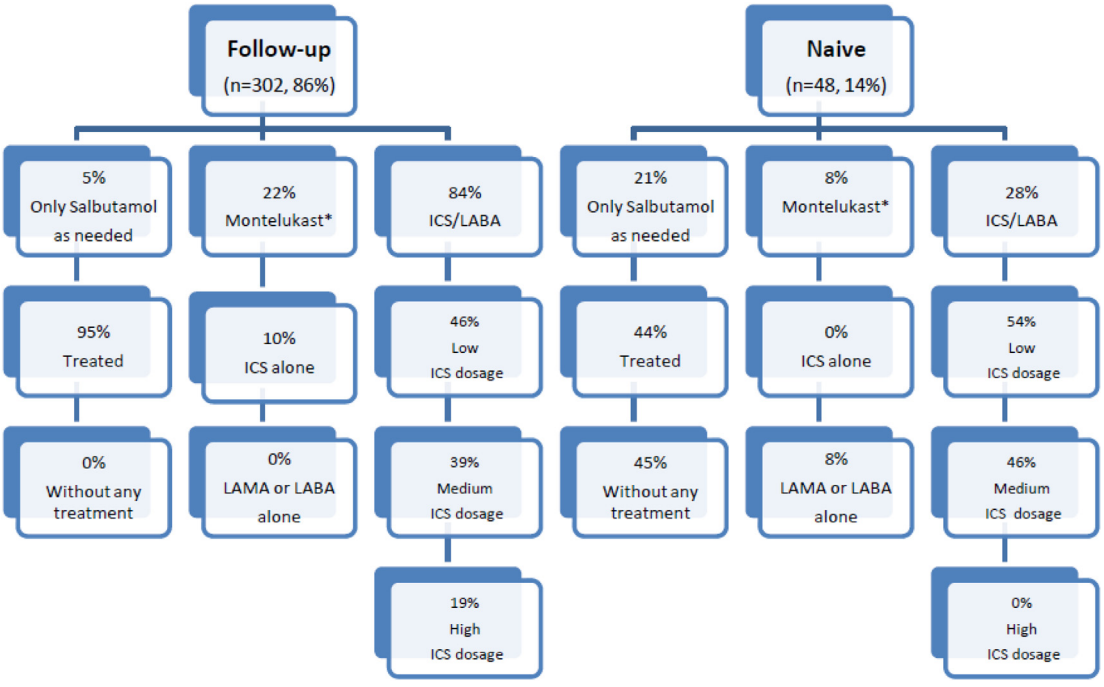

Fig. 1 Follow up and naïve subjects respiratory therapies. LAMA, Long Acting Muscarinic Antagonist. Montelukast was taken mainly as add on therapy (86% and 100% in the two groups, respectively).

Table 2 Demographic, clinical and functional data comparisons between asthma and Asthma-COPD Overlap Syndrome (ACOS).

	Asthmatic ($n = 249$)	ACOS ($n = 101$)	*P*
Female, %	63	63	0.903
Age, years	72 ± 5	74 ± 5	0.014
BMI, kg/m^2	28 ± 5	27 ± 5	0.274
BMI≥30, %	26	21	0.203
Current smokers, %	4	3	<0.001
Former smokers, %	21	40	
Never smokers, %	74	56	
Pack-years	16 ± 12	16 ± 11	0.970
Age of onset, yrs	57 ± 17	57 ± 21	0.959
Asthma duration, yrs	15 ± 17	16 ± 20	0.491
Sensitized, %	52	52	1.000
mMRC, score	0.99 ± 0.84	1.26 ± 0.98	0.010
ACT, score	21 ± 4	18 ± 4	<0.001
Subjects with SAE,%	18	42	<0.010
Subjects with ≥2 SAEs, %	7	25	<0.010
ACT score ≤19, %	28	50	<0.0010
FEV_1/FVC, % predicted	89 ± 12	85 ± 11	0.005
FEV_1, % predicted	85 ± 20	78 ± 20	0.001
FVC, % predicted	95 ± 16	91 ± 16	0.016
Comorbidity, %	68	80	0.026
Two comorbidities, %	41	45	0.633
≥3 comorbidities, %	12	16	0.383

Data are expressed ad mean ± SD if not otherwise stated. Sensitized: to airborne allergens. mMRC: modified Medical Research Council dyspnea score; SAE, Severe Asthma Exacerbation; ACT: Asthma Control Test.

subjects on follow-up versus those on first visit did not differ between ACOS and asthma (87% vs 83% and 13% vs 17%, respectively). Subjects with ACOS and asthma underwent similar treatments, with the exception of a more frequent use of tiotropium (25% vs 3%, respectively; $p < 0.01$), a less frequent use of the ICS/LABA combination (63% vs 82%, respectively; $p < 0.001$), and with a higher ICS dosage (30% vs 15%, respectively; $p = 0.04$) in the former. Similarly, the percentage of patients without any treatment did not differ between subjects with ACOS and asthma (8% vs 7%, respectively). The percentage of those on high intensity treatments (step 4, high ICS/LABA or medium ICS/LABA plus montelukast) who achieved control of their asthma was not different between those with ACOS and asthma (23% vs 18%, respectively). A non-significant result was also found for those with ACOS and asthma who had an ACT score of ≤19 (14% vs 8%, respectively).

Non respiratory therapies

Subjects with ACOS more frequently took at least one non-respiratory drug for another disease compared to subjects with asthma (80% vs 66%, $p = 0.008$). The distribution of comorbidities between the two groups is summarized in Table 3, showing a less frequent use of drugs for gastro-esophageal reflux in subjects with ACOS. The percentage of subjects with two or more comorbidities did not differ between the two groups (45% vs 41%). None of the subjects with ACOS and only 3 subjects with asthma were receiving treatment with a β-blocking medication.

Factors affecting asthma control

A multivariate linear regression analysis was performed using the ACT score as the dependent variable in a stepwise fashion to explore which factors influenced the lack of asthma control in elderly asthmatics. As shown in Table 4, the only variables that remained significant were the FEV_1% of predicted, mMRC score and occurrence of ACOS.

Discussion

The main findings of our study are: 1) more than one-third of elderly asthmatic patients had uncontrolled asthma, despite using GINA steps 3–4 antiasthmatic therapy; 2) one-third of elderly asthmatics showed features of COPD; and 3) elderly asthmatics with COPD had worse control of the disease.

Asthma control

The well-known trend towards poor control of asthma in the elderly [1] is confirmed in our study by the fact that an ACT score ≤19 and one SAE in the previous year was seen in 39% and 25% of subjects, respectively. One of the possible explanations could lie in the high proportion of cigarette smoke exposure in elderly asthmatics. In the current study, almost 30% of the patients were former smokers; their percentage was significantly lower in females than in males. However, the relationship between smoking habits and asthma is not clear. According to some observations [22], persistent smoking exposure is associated with a remission of asthmatic symptoms, perhaps because of the occurrence of a state of "resistant" airways to the inflammatory effects of smoke. On the other hand, susceptible airways lead to avoidance of smoke or quitting smoking. In this regard, quitting smoking has been associated with the

Table 3 Distribution of drugs for non respiratory diseases in asthma and Asthma-COPD Overlap Syndrome (ACOS).

	Asthma ($n = 249$)	ACOS ($n = 101$)	*P*
Arterial hypertension, %	53	66	0.024
Gastroesophageal reflux, %	30	23	0.152
Osteoporosis, %	18	25	0.140
Diabetes, %	16	20	0.349
Chronic heart disease, %	15	14	0.869

Table 4 Clinical and functional variables of patients according to asthma control.

	Level of asthma control			*P*
	Well controlled	Partially controlled	Poorly controlled	
N (%)	184 (61%)	82 (27%)	37 (12%)	
Age, yrs	73 ± 5	72 ± 5	72 ± 7	0.860
F, %	58	62	73	0.234
BMI, kg/m^2	27.4 ± 5.0	27.4 ± 4.5	26.7 ± 5.5	0.742
BMI≥30, (%)	23	26	24	0.883
Current smokers, %	4	4	3	0.599
Former smokers, %	29	27	16	
Never smokers, %	67	69	81	
Pack-years	16 ± 11	18 ± 12	17 ± 14	0.655
Age of onset, yrs	56 ± 17	55 ± 19	49 ± 22	0.096
Asthma duration, yrs	17 ± 16	17 ± 19	23 ± 23	0.118
Sensitized, %	47	54	57	0.437
mMRC, score	0.72 ± 0.71	1.38 ± 0.80	2.03 ± 0.90	<0.001[a]
Subjects with SAE,%	20	41	40	<0.001[b]
FEV_1, % predicted	87 ± 20	77 ± 19	75 ± 22	<0.001[b]
FVC, % predicted	97 ± 15	89 ± 15	90 ± 17	<0.001[b]
ACOS, %	19	43	43	<0.001[b]
Comorbidity, %	70	80	70	0.172
Two comorbidities, %	40	51	43	0.247
≥3 comorbidities, %	12	22	11	0.103
Arterial hypertension, %	56	60	59	0.864
Gastroesophageal reflux,%	26	35	27	0.255
Osteoporosis, %	16	28	27	0.057
Diabetes, %	15	21	16	0.469
Chronic heart disease, %	18	16	11	0.557

Data are expressed ad mean ± SD if not otherwise stated. Level of asthma control: well, partially and poorly controlled for ACT (asthma control test) score ≥20, 16–19, or ≤15, respectively. Sensitized: to airborne allergens. mMRC: modified Medical Research Council dyspnea score; SAE, Severe Asthma Exacerbation.

[a] All the differences between groups are statistically significant.

[b] Only the difference between well vs partially and well vs poorly controlled are statistically significant.

remission of asthmatic symptoms [23,24]. In the multivariate analysis, however, smoking exposure did not appear to influence the lack of asthma control (Table 4).

Females were more represented than males, possibly because of an increased prevalence of female subjects in the older population due to their increased longevity. In our study, females reported more breathlessness than males as measured by the mMRC scale, as also reported by others [25,26]. They also had significantly lower ACT scores, another result reported by other studies [27,28], although a recent paper did not replicate these findings [29]. However, in the multivariate analysis, gender did not hold up as an independent variable affecting asthma control.

It is noteworthy that 39% of our patients had uncontrolled asthma despite receiving a high level GINA therapy (steps 3–4) [10], and only 8% of them were not receiving any treatment. Possible explanations for the lack of asthma control in our elderly patients could be the well-known poor perception of dyspnea in the elderly [30] and/or a lower adherence to therapy and/or improper use of inhaler devices [1,3,31,32]. Indeed, the level of dyspnea perception (as assessed by the MRC scale) was the most significant factor affecting asthma control in our study population. In a recent prospective longitudinal study aimed at assessing asthma remission and control, asthma was controlled in only 28% of patients, while 41% had partially controlled asthma and 31% had uncontrolled asthma [33]. A 64% prevalence of uncontrolled asthma in patients over 18 years of age was also reported by other authors [34]. We are confident that our patients, who were receiving regular clinical follow-ups, received proper instruction and were regularly tested for their inhalation techniques, although the lung function of our patients was less impaired than that reported in the Rochester study [35].

Half of the subjects were sensitized to aeroallergens, mainly HDM. Although asthma in older patients is thought to be predominantly non-atopic, recent studies report a sensitization rate ranging from 30 to 75% [36,37], mainly for indoor allergens [38]. A recent large population study on asthma prevalence [39] reported a sensitization rate of approximately 65% in older asthmatics, which is not significantly different from what is observed in younger asthmatics. Interestingly, a total of 9% of our study population had HDM sensitization and poorly controlled asthma (ACT ≤ 19), becoming potential candidates for anti-IgE therapy [10]. As suggested by Scichilone et al. [40], evaluation of allergic sensitization should be recommended for elderly asthmatic patients. Another intriguing finding from our survey is related to the onset of asthma. Most of our

patients received a diagnosis of asthma within the previous 10 years, similar to what was reported in the Rochester study [35]. We are aware of possible recall bias, which appears less probable in our survey because our patients had received diagnoses by their physicians and were receiving regular follow-ups for asthma. This is in contrast to surveys that use telephone questionnaires or self-reported diagnoses of asthma.

Asthmatics may demonstrate a fixed airway obstruction and develop features similar to COPD over time [41,42]. The definition of ACOS is still a matter of debate [8,43], and the 2014 update of the GINA guidelines, published during the revision of this manuscript, provides a consensus-based approach to distinguishing between asthma, COPD, and ACOS, rather than attempting to create a formal definition of ACOS [44]. In a recent epidemiological Italian study on the general population [45], aging was associated with a marked decrease in the prevalence of diagnosed asthma and with a marked increase in the prevalence of diagnosed COPD. According to this study, the percentage of asthma-COPD overlap was as high as 61% among the asthmatic subjects who were over 65 years old. Fifteen percent of North Carolina adults reported a history of COPD and/or asthma and 2.4% reported both [46]. In our study population, ACOS was observed in 29% of patients, which is lower than the 40% prevalence reported by Soriano et al. [6] and similar to that reported by Oraka et al. [47].

In our study population, patients with ACOS had worse asthma control, in terms of an ACT score of $\leq$19 or the occurrence of SAEs in the previous year, compared to asthmatic patients. Hardin et al. [48] reported worse control in patients with COPD, when they had a history of physician-diagnosed asthma, showing a higher exacerbation rate (33% vs 18%), similar to the exacerbation rate observed in our study of patients with ACOS. However, the two studies are not comparable, because we assessed whether the coexistence of COPD in asthma impairs its control and not *vice versa*. According to a recent study [49], chronic bronchitis is a risk factor for COPD exacerbations, and this could be an additional explanation for the high prevalence of exacerbations in our overlap patients.

Finally, the higher prevalence of exacerbations that we observed in patients with ACOS may be related to comorbidities, which were more commonly reported in these patients (82% vs the 68% observed in asthmatic patients, $p < 0.001$, respectively), in agreement with previous reports [46,50]. It is largely accepted that comorbidities in older patients make managing their asthma a highly demanding task [51].

Some caveats should be considered in the interpretations of our results. First, we performed the CO diffusion test only in subjects with fixed airway obstructions and/or smoking habits. This could underestimate the ACOS prevalence, in that subjects with smoking habits and fixed airway obstructions, but normal CO diffusion tests, could be considered to be affected by COPD and not by asthma [11]. However, because we found only 6 subjects with these characteristics, their misclassification can be considered negligible. Second, we did not assess airway inflammation (i.e., induced sputum or exhaled nitric oxide levels in the expired air), which could help to distinguish COPD from ACOS [52]. Third, we cannot exclude that chronic coughing and phlegm are simply clinical aspects of asthma [33,53,54].

In conclusion, we found that more than one-third of elderly asthmatic patients had uncontrolled asthma, despite GINA steps 3—4 antiasthmatic therapy. Our results highlight the need to specifically address the association with COPD, which was related to worse asthma control.

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